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Clinical factors associated with postictal headache in Chinese patients with partial epilepsy

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ABSTRACT

Purpose: To investigate the incidence of postictal headache (PIH) and the factors potentially related to the occurrence of PIH in a Chinese epileptic center.
Methods: Consecutive adult patients with epilepsy, referred to the outpatient clinic of the Epilepsy Center of the PLA General Hospital between February 01, 2012, and May 10, 2013, were recruited to this study. 854 patients with partial epilepsy completed a questionnaire regarding headache, 466 patients with temporal lobe epilepsy (TLE), 82 patients with occipital lobe epilepsy (OLE) and 306 patients with frontal lobe epilepsy (FLE). A semi-structured interview was performed in those who confirmed headache.
Results: PIH occurred in 328 (38.41%) of the subjects. By type of epilepsy, PIH was found in 164 (35.19%) of the patients with TLE, 46 (56.01%) of the patients with OLE, and 118 (38.56%) of the patients with FLE. The incidence of PIH in OLE was significantly higher than in TLE and FLE ($P < 0.05$). It occurs more frequently after generalized tonic–clonic seizures than other seizure types. Logistic regression analysis revealed that age at onset, type of seizure and classification of epilepsy were each significantly related to the occurrence of PIH.
Conclusion: The results of our study revealed possible relationships between PIH and the region of epileptic focus and area of spread of epileptic discharges.

1. Introduction

Epilepsy and headache are all paroxysmal disorders. Headache is one of the comorbidities that may add to the burden of epilepsy. The association between headaches and seizure disorders has long been debated and is still poorly understood. In clinical practice, patients with epilepsy not infrequently complain of headaches, clinicians often fail to explicitly ask the patients about seizure-associated headache. Headache may be temporally linked to seizures in different ways. It may occur prior to a seizure (preictal headache), during a seizure (ictal headache), after a seizure (postictal headache, PIH) or be unrelated to seizures (interictal headache).[1–3] Postictal and interictal headaches are common with a frequency of 35–51% and 31–64%, respectively.

The relationship between type of epilepsy and PIH is also of interest. It is suggested that seizures can trigger secondary headache attacks (postictal headache).[4,5] It has been pointed out that generalized tonic–clonic seizure (GTCS) is associated with PIH.[6,7] Other researchers have also noted that OLE is often associated with headaches.[8–10] These findings suggest that the underlying mechanism of PIH may be related to seizure type and the location of epilepsy. However, very few studies have addressed this issue, especially in China.

The purpose of this study was to determine the incidence of PIH and to investigate factors potentially related to the occurrence of PIH. We therefore compared the incidences of PIH and examined clinical factors possibly related to PIH for three types of localization-related epilepsy, i.e. TLE, OLE, and FLE.

2. Methods

Consecutive adult patients with epilepsy, referred to the outpatient clinic of the Epilepsy Center of PLA General Hospital between February 01, 2012, and May 10, 2013, were recruited to this study. All patients had a definite diagnosis of epilepsy seen by at least two epileptologists. Diagnoses were made according to the International League Against Epilepsy classification[11] on the basis

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of clinical symptoms, electroencephalography (EEG), and magnetic resonance imaging (MRI). Seizures were classified as simple partial seizure (SPS) and/or complex partial seizure (CPS), mixed SPS and generalized tonic–clonic seizure (GTCS), and mixed CPS and GTCS.

Patients included in this study were 18 years-old or more and with intact ability to answer the questionnaires. Patients with mental retardation, learning disability, behavioral disorder or other evident abnormalities that could compromise the cooperation to respond the questionnaires were excluded. In those who confirmed headaches, a standardized semistructured telephone interview was performed, with questions about timing of headache in relation to seizures, in addition to frequency, duration, intensity, localization, and associated features of the headaches.[12,13] In this study, postictal headache as a headache starting within three hours after a seizure and ceasing within 72 h after the attack.[12] Informed consent was obtained from all subjects.

The patients were asked to grade the usual headache intensity as mild (maintaining normal activities without problems), moderate (maintaining normal activities with difficulty), severe (must give up normal activities and lie down) or extremely severe (impossible to stay still). Further diagnostic questions were based on ICHD-II criteria[12] and aimed to identify migraine and tension-type headache (TTH). The medical chart of each patient was reviewed to ascertain clinical factors such as age at onset of epilepsy, duration of illness, type of seizures, and number of antiepileptic drugs (AEDs) taken.

All analyses were performed using SPSS version 14.0. For statistical analysis, we used one-way analysis of variance (ANOVA) to determine the significance of differences in clinical factors among the three groups. Continuous variables were summarized as means and standard deviations, and categorical variables as numbers and percentages. Chi-square was used to compare distributions of categorical variables between groups; the paired-sample *t*-test and ANOVA were used to compare continuous variables. Statistical significance was set at $P < 0.05$. Logistic regression analysis with stepwise elimination method was used to test for relationship between each potential risk factor and the occurrence of PIH.

3. Results

3.1. Incidence of seizure-associated headache among patients with partial epilepsy:

854 patients with partial epilepsy (464 men and 370 women, average age 31.06 ± 11.92 years) from our epilepsy outpatient clinic were prospectively interviewed by questionnaire as to whether or not they suffer from headaches associated with epileptic seizures. Including 466 patients with TLE, 306 patients with FLE, and 82 patients with OLE.

Table 1 shows the clinical characteristics of the subjects. There were no significant differences in age, age at onset, seizure type, a history of interictal headaches, duration of illness or number of AEDs among the three epilepsy groups.

Table 1
Clinical features of subjects.

	FLE $n = 306$	TLE $n = 466$	OLE $n = 82$
Sex			
Female	138	212	40
Male	168	254	42
Age, year (mean)	32.92 ± 12.60	32.87 ± 12.16	31.49 ± 6.22
Age at onset, year (mean)	23.52 ± 13.64	22.70 ± 13.81	21.50 ± 8.98
Duration of epilepsy, year (mean)	9.35 ± 8.24	10.08 ± 8.96	10.03 ± 7.22
Seizure type			
SPS/CPS	34	172	4
SPS + GTCS	154	12	4
CPS + GTCS	118	282	74
A history of interictal headaches	22	26	12
Number of AEDs (mean)	1.28 ± 0.70	1.31 ± 0.82	1.22 ± 0.85

TLE, temporal lobe epilepsy; FLE, frontal lobe epilepsy; SPS, simple partial seizure; CPS, complex partial seizure; GTCS, generalized tonic–clonic seizure; AEDs, antiepileptic drugs.

PIH occurred in 328 (38.41%) of the subjects. By type of epilepsy, PIH was found in 164 (35.19%) of the patients with TLE, 118 (38.56%) of the patients with FLE, and 46 (56.01%) of the patients with OLE. The incidence of PIH in OLE was significantly higher than in TLE and FLE ($P < 0.05$), although there was no significant difference in incidence between TLE and FLE.

We examined clinical factors including sex, age at onset, duration of illness, type of seizure, classification of epilepsy, a history of interictal headaches and number of AEDs. Logistic regression analysis revealed that age at onset, type of seizure and classification of epilepsy were each significantly related to the occurrence of PIH (Table 2). The risk of occurrence of PIH was significantly greater with younger age at onset and for patients with GTCS. The OLE group had a significantly higher risk for PIH than did the TLE and FLE groups. Other factors were not significantly related to the occurrence of PIH.

3.2. Postictal headaches

Postictal headaches were most common after generalized tonic–clonic seizures 270 of 374 patients (72.19%), but were also reported by 58 of 152 patients (38.16%) after partial seizures without generalization. There was no correlation between the duration and severity of partial and that of headaches.

The headache was graded as mild in 90 (27.44%), moderate in 194 (59.15%), severe in 44 (13.41%), no patient suffered as extremely severe (Table 3). According to the ICHD-II criteria, postictal headaches were classified as migraine in 200 patients (60.98%). 24 patients' headaches were classified as "migraine-like",

Table 2
Clinical factors related to the occurrence of postictal headaches.

	Post-ictal headaches	Odd ratio	95% CI	*P*
Age at onset	19.16 ± 10.42	0.896	0.876–0.926	0.036
Duration of illness	10.33 ± 8.12	0.961	0.928–1.003	0.079 (NS)
Epilepsy type				
OLE	46 (56.01%)	1		
TLE	164 (35.19%)	0.312	0.113–0.869	0.019
FLE	118 (38.56%)	0.341	0.098–0.789	0.026
Seizure type				
With GTCS	270	1		
Without GTCS	58	0.385	0.156–0.847	0.0002
A history of interictal headaches	32 (9.76%)	0.971	0.918–1.012	0.083 (NS)
Number of AEDs	1.36 ± 0.80	1.25	0.983–1.971	0.069 (NS)

Table 3
Clinical characteristics of epilepsy-related headaches.

Headache	FLE ($n=118$)		TLE ($n=164$)		OLE ($n=46$)	
	n	%	*n*	%	*n*	%
Intensity						
Mild	36	30.51	44	26.83	10	21.74
Moderate	68	57.63	100	60.97	26	56.52
Severe	14	11.86	20	12.20	10	21.74
Accompanying symptoms						
Nausea	72	61.02	106	64.63	32	69.56
Vomiting	29	24.58	57	34.76	18	39.13
Photophobia	25	21.19	48	29.27	12	26.09
Phonophobia	23	19.49	45	27.44	13	28.26
Aggravation by moderate physical activity	21	17.80	50	30.49	21	45.65
Quality						
Pulsating	70	59.32	108	65.85	32	69.57
Pressing/tightening	28	23.73	31	18.90	8	17.39
Other	13	11.02	16	9.76	4	8.70
Uncertain	7	5.93	9	5.49	2	4.35
Fulfilling migraine criteria of ICHD-II	66	55.93	103	62.80	31	60.17
Mean duration of headache (h)	14.02 ± 15.67		16.22 ± 22.88		18.20 ± 21.30	

because they lasted less than 4 h and for this reason only did not fulfill the ICHD-II criteria for migraine. Postictal tension-type headache was reported by 67 patients (20.43%). In 37 patients (9.89%), headaches could not be classified according to ICHD-II criteria.

3.3. Treatment of postictal headaches

No patient treated headache according to a medical prescription or used over-the-counter analgesics.

3.4. Comparison of epileptic syndrome and postictal headache syndrome

Of 102 patients with unilateral headaches after partial seizures, 49 had headaches ipsilateral to the epileptogenic focus and 31 had headaches contralateral to the epileptogenic focus. The side of the epileptic focus was not identified in 22 patients with unilateral headache syndrome after partial seizures.

3.5. Headache not associated with epileptic seizures

268 patients reported no other relevant headaches. 42 patients had typical attacks of migraine without aura not associated with seizures. 14 patients had episodic tension-type headache not associated with the seizures. 4 patients reported other headache syndromes that could not be classified (Table 4).

Table 4
Characteristics of patients with seizure-related headaches and Headache not associated with epileptic seizures.

Epileptic syndrome	Seizure-related HA	Number of AED (n)	Not seizure-related HA
Temporal lobe	164	0 AED 18 1 AED 66 2 AED 66 3 AED 12 4 AED 2	Migraine 20 Tension-type headache 4 Not classified 2
Frontal lobe	118	0 AED 12 1 AED 72 2 AED 32 4 AED 2	Migraine 14 Tension-type headache 6 Not classified 2
Occipital lobe	46	0 AED 8 1 AED 20 2 AED 14 3 AED 4	Migraine 8 Tension-type headache 4 Not classified 0

HA: headache.

4. Discussion

The overall incidence of PIH in this study was 38.41%, the high incidence of postictal headaches agrees with previously published data. According to data from the literature, the incidence of postictal headaches range between 13% and 52%.[14] The variation in incidence of PIH found among previous studies may have been due to differences in type of epilepsy examined, because the subjects were not appropriately classified in most of those reports. However, our study showed that the incidence varied among the three types of epilepsy: 35.19% in TLE, 56.01% in OLE, and 38.56% in FLE. Our results again showed that OLE had the highest risk for PIH, the incidence of PIH was higher for OLE than for TLE and FLE.

In several studies,[9,15,16] headaches were observed in patients with occipital lobe seizure or EEG abnormality in the occipital region. These findings suggest that certain kinds of epilepsy are often associated with PIH. The region of focus may thus play an important role in induction of PIH. Our study did not address this topic, and the number of patients with defined occipital lobe syndromes was small for further statistical analysis.

It is interesting to observe the difference of PIH after GTCS and CPS in this study, patients with GTCS had a high risk for PIH, which in contrast with that reported in children in a multicentric study.[17] Our findings are consistent with those researchers[14] who have suggested that GTCS is more often associated with PIH than other types of seizure. It has been speculated that changes in blood flow after GTCS may trigger PIH. However, the finding that CPS can also be followed by headaches suggests that other mechanisms may also participate in PIH.

Postictal migraine-type headache (60.98%) and tension-type headache (20.43%) were the most common type of headache. This findings agreed with an explanation for the pathophysiology of PIH is similar to migraine pathophysiology. The classic publication of Schon and Blau[1] on postictal headache and migraine states that all patients with postictal headaches have at least one characteristic of migraine such as vomiting, photo-, or phonophobia. Therefore, the authors suggest that, as postulated for migraine, postictal headaches might also be related to the vasodilatation known to follow seizures. Therefore, conclusive pathophysiological concepts of postictal headaches cannot yet be proposed.

Younger age at onset of epilepsy was also found to be an important risk factor in PIH in this study. There have been fewer reports referring to a relationship between age at onset of epilepsy and PIH. Since duration of illness was not found to be a risk factor for PIH, the prolonged course of epilepsy is unlikely to explain this phenomenon. Some researchers have speculated that there are possible effects of epileptic discharges on immature brain in the occurrence of PIH. Some studies have showed that there are higher incidence of headache in children.[18] However, it would be difficult to draw the conclusion from the present data. More studies will be needed to confirm this finding.

Although cortical spreading depression (CSD) has been shown to activate the trigeminovascular system, whether seizures or CSD causes true migraine typical attack remains a matter of debate. Nevertheless, CSD seems to be the connecting point between migraine and epilepsy.[19–22]

How CSD and epileptic discharges can, in more detail, facilitate each other, although with different degree and efficiency? In other words, why could the onset of epileptic seizure facilitate the onset of CSD to a greater degree than the onset of CSD facilitating the onset of epileptic seizure? Which has been demonstrated in several studies, in particular, Parisi et al., have suggested how the etiopathogenetic mechanism linking an epileptic focus and cortical spreading depression may work.[23,24] They stressed that a migraine/headache attack can originate at either the cortical or subcortical level, whereas an epileptic focus arises cortically and can only be modulated at the subcortical level.[25,26]

Two mechanisms have been hypothesized by Parisi et al. to explain headache/migraine as a sole "ictal epileptic manifestation": (1) a subclinical epileptic discharge might activate the trigeminovascular system, resulting in a migraine/headache without any other associated cortical epileptic sign or symptom; (2) central autonomic networks (whether cortical or subcortical) have a lower threshold for epileptogenic activation than those that produce a focal cortical semiology.[27,28] For example, in the Panayiotopoulos syndrome, ictal epileptic autonomic symptomatology appears to pertain to any epileptogenic cortical onset zone, be it occipital, frontotemporal or frontal. Therefore, seizures might remain purely autonomic if ictal neuronal activation of non-autonomic cortical areas fails to reach the symptomatogenic threshold.[17] This possible mechanism, first suggested for the Panayiotopoulos syndrome, might represent another mechanism that leads to headache/migraine as a sole "ictal epileptic manifestation". It should be stressed that, as occurs for autonomic manifestations (vomiting, tachycardia, etc.), children are far more likely to develop migraine as the sole epileptic manifestation than adults. Why the occipital lobe stimulates autonomic symptoms and signs to a much greater extent than other cortical areas is still unknown. Although a correlation between the microstructure and function of an area and its connections has been established for many cortical regions, particularly for primary sensory and motor areas, very little is as yet known about the anatomofunctional pathways linking the cerebral cortex and cortico-subcortical vegetative/autonomic neural networks. This point of view by Parisi P has been strongly supported by data in cerebral human tissue,[29] demonstrating how epileptic focus and CSD can facilitate each others. Moreover, in the last decade, the roles of CSD and trigeminovascular system (TVS) activation in the physiopathology of migraine have been clearly documented. Epileptic discharges and CSD stimulate each other in experimental conditions. Parisi et al. suggested that the threshold required for the onset of CSD can be lower than that required for an epileptic seizure.[30] In other words, the onset of epileptic seizure may facilitate the onset of CSD to a greater degree than the onset of CSD facilitates the onset of epileptic seizure. As stated by Parisi et al.,[31] this may explain why, in the clinical context, we are more likely to observe epileptic patients with "comorbid" (peri-ictal and inter-ictal) migraine than migraine subjects with "comorbid" epilepsy. In this respect, we would like to have a deeply experimental and clinical research on this topic in the future.

Our study showed that although 72.56% of our patients indicated that their postictal headaches were moderate to severe, the patients hesitate to treat their headaches for fear of having to take more tables, and their doctors do not ask them about headaches and therefore do not advise them of appropriate treatment. No patient treated postictal headaches according to a doctor's prescription. This observation reflects the underestimation of postictal headaches in physicians treating patients with epilepsy, which was similar with Parisi et al. has certainly reported that the comorbidity between headache and epilepsy can often be neglected by epileptic patients and their physicians, probably why "the epileptic picture" "overshadow" the "headache events".

5. Reliability of the study

This study is based on a prospective analysis, and focus on the incidence of PIH in three partial epilepsy, which the subjects were not appropriately classified in most of previous reports. The total number of the patients are the largest according to our knowledge. The major limitation of this study is this was a questionnaire based investigation about the characteristics of postictal headache in patients with partial epilepsy, so the accuracy of some data may be poor. We did not include an EEG recording of peri-ictal phase, nor in particular of the "post-ictal" headache phase, which could not be able "to demonstrate or routed out" if "PIH" cases could be or not an "ictal epileptic headache" (cases where headache can be the sole ictal epileptic manifestation).[32] There has the relatively small numbers of patients with OLE which limits the power of this investigation, especially to further analyses the effects of EEG and MRI abnormal in the occipital region.

6. Conclusion

To the best of our knowledge, our study is the first one that demonstrated the clinical factors associated with postictal headache in Chinese patients with partial epilepsy. The results of our study revealed possible relationships between PIH and the region of epileptic focus and area of spread of epileptic discharges. Further studies of a larger number of subjects will be required to evaluate our findings, and the whole migraine/headache and epilepsy spectrum relationships, taking into account and mentioning the new and recent findings such as the new "Ictal Epileptic Headache" concept and the published criteria which have even been more recently mentioned in the "appendix" of the new edition (third edition) of the ICHD-3, published in Cephalalgia.[33]

Conflicts of interest statement

None declared.

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References

1. Schon F, Blau JN. Post-epileptic headache and migraine. *J Neurol Neurosurg Psychiatry* 1987;**50**(9):1148–52.
2. Bernasconi A, Andermann F, Bernasconi N, Reutens DC, Dubeau F. Lateralizing value of peri-ictal headache: a study of 100 patients with partial epilepsy. *Neurology* 2001;**56**(1):130–2.

3. HELP Study Group. Multi-center study on migraine and seizure-related headache in patients with epilepsy. *Yonsei Med J* 2010;**51**(2):219–24.
4. Forderreuther S, Henkel A, Noachtar S, Straube A. Headache associated with epileptic seizures: epidemiology and clinical characteristics. *Headache* 2002;**42**(7):649–55.
5. Botha SS, Schutte CM, Olorunju S, Kakaza M. Postictal headache in South African adult patients with generalised epilepsy in a tertiary care setting: a cross-sectional study. *Cephalalgia* 2010;**30**(12):1495–501.
6. Bauer PR, Carpay JA, Terwindt GM, Sander JW, Thijs RJ, Haan J, et al. Headache and epilepsy. *Curr Pain Headache Rep* 2013;**17**(8):351.
7. Ito M, Adachi N, Nakamura F, Koyama T, Okamura T, Kato M, et al. Characteristics of postictal headache in patients with partial epilepsy. *Cephalalgia* 2004;**24**(1):23–8.
8. Andermann F, Zifkin B. The benign occipital epilepsies of childhood: an overview of the idiopathic syndromes and of the relationship to migraine. *Epilepsia* 1998;**39**(Suppl. 4):S9–23.
9. Walker MC, Smith SJ, Sisodiya SM, Shorvon SD. Case of simple partial status epilepticus in occipital lobe epilepsy misdiagnosed asmigraine: clinical, electrophysiological, and magnetic resonance imaging characteristics. *Epilepsia* 1995;**36**(12):1233–6.
10. Ogunyemi A, Adams D. Migraine-like symptoms triggered by occipital lobe seizures: response tosumatriptan. *Can J Neurol Sci* 1998;**25**(2):151–3.
11. Commission on classification and terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;**30**(4):389–99.
12. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders: 2nd ed.. *Cephalalgia* 2004;**24**(Suppl. 1):9–160.
13. Yu S-Y, Cao X-T, Zhao G, Yang X-S, Qiao X-Y, Fang Y-N, et al. The burden of headache in China: validation of diagnostic questionnaire for a population-based survey. *J Headache Pain* 2011;**12**(2):141–6.
14. Ito M, Nakamura F, Honma H, Takeda Y, Kobayashi R, Miyamoto T, et al. Clinical factors associated with postictal headache in patients with epilepsy. *Acta Neurol Scand* 2000;**102**(2):129–31.
15. Melchionda D, Verrotti A, Chiarelli F, Domizio S, Sabatino G, Mucedola T, et al. Headache in children with centrotemporal spikes. *Neurophysiol Clin* 1999;**29**(1):90–100.
16. Ito M, Nakamura F, Honma H, Takeda Y, Kobayashi R, Miyamoto T, et al. A Comparison of postictal headache between patients with occipital lobe epilepsy and temporal lobe epilepsy. *Seizure* 1999;**8**(6):343–6.
17. Verrotti A, Coppola G, Spalice A, Di Fonzo A, Bruschi R, Tozzi E, et al. Peri-ictal and inter-ictal headache in children and adolescents with idiopathic epilepsy: a multicenter cross-sectional study. *Childs Nerv Syst* 2011;**27**(9):1419–23.
18. Kelley SA, Hartman AL, Kossoff EH. Comorbidity of migraine in children presenting with epilepsy to a tertiary care center. *Neurology* 2012;**79**(5):468–73.
19. Fabricius M, Fuhr S, Willumsen L, Dreier JP, Bhatia R, Boutelle MG, et al. Association of seizures with cortical spreading depression and peri-infarct depolarisations in the acutely injured human brain. *Clin Neurophysiol* 2008;**119**(9):1973–84.
20. Eikermann-Haerter K, Ayata C. Cortical spreading depression and migraine. *Curr Neurol Neurosci Rep* 2010;**10**(3):167–73.
21. Eikermann-Haerter K, Negro A, Ayata C. Spreading depression and the clinical correlates of migraine. *Rev Neurosci* 2013;**24**(4):353–63.
22. De Simone R, Ranieri A, Montella S, Bonavita V. Cortical spreading depression and central pain networks in trigeminal nuclei modulation: time for an integrated migraine pathogenesis perspective. *Neurol Sci* 2013;**34**(Suppl. 1):S51–5.
23. Parisi P. Why is migraine rarely, and not usually, the sole ictal epileptic manifestation? *Seizure* 2009;**18**(5):309–12.
24. Parisi P, Striano P, Verrotti A, Villa MP, Belcastro V. What have we learned about ictal epileptic headache? A review of well-documented cases. *Seizure* 2013;**22**(4):253–8.
25. Kasteleijn-Nolst Trenité DG, Verrotti A, Di Fonzo A, Cantonetti L, Bruschi R, Chiarelli F, et al. Headache, epilepsy and photosensitivity: how are they connected? *J Headache Pain* 2010;**11**(6):469–76.
26. Belcastro V, Striano P, Kasteleijn-Nolst Trenité DG, Villa MP, Parisi P. Migralepsy, hemicrania epileptica, post-ictal headache and ictal epileptic headache: a proposal for terminology and classification revision. *J Headache Pain* 2011;**12**(3):289–94.
27. Verrotti A, Striano P, Belcastro V, Matricardi S, Villa MP, Parisi P. Migralepsy and related conditions: advances in pathophysiology and Classification. *Seizure* 2011;**20**(4):271–5.
28. Verrotti A, Coppola G, Di Fonzo A, Tozzi E, Spalice A, Aloisi P, et al. Should migralepsy be considered an obsolete concept? A multicenter retrospective clinical/EEG study and review of the literature. *Epilepsy Behav* 2011;**21**(1):52–9.
29. Berger M, Speckmann EJ, Pape HC, Gorji A. Spreading depression enhances human neocortical excitability in vitro. *Cephalalgia* 2008;**28**(5):558–62.
30. Parisi P, Striano P, Negro A, Martelletti P, Belcastro V. Ictal epileptic headache: an old story with courses and appeals. *J Headache Pain* 2012;**13**(8):607–13.
31. Parisi P, Striano P, Belcastro V. The crossover between headache and epilepsy. *Expert Rev Neurother* 2013;**13**(3):231–3.
32. Parisi P, Striano P, Trenité DG, Verrotti A, Martelletti P, Villa MP, Belcastro V. 'Ictal epileptic headache': recent concepts for new classifications criteria. *Cephalalgia* 2012;**32**(9):723–4.
33. The International Classification of Headache Disorders, 3rd ed. (beta version), 2013;33(9):629–808 [p. 801].